

REPLACEMENT SHEET

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Title: RATIONAL EVOLUTION OF CYTOKINES FOR HIGHER STABILITY,
THE CYTOKINES AND ENCODING NUCLEIC ACID MOLECULES

Applicants: Rene Gantier et al. Attorney Docket No. 17109-012001/922

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Cytokine regions susceptible to protease attack identified by structural alignment with Lead mutants

of IFN α -2b

IFN- α 2b CDLPQTHSLGSRRTIMLLAQMRKISLFSCLKDRHDFGFPQEEFGNQFQAKETIPVLHEMIQOIFNLFSTKDSAAWDETLIDKRYTELYQOLNDLEACVIGQ

VGVTETPLMKEDSILA VRKYFORITLYIKKKYSPCAMEVVRRAETMRSPSLSTNIQESLRSE

Exemplary protein of the interferons/interleukin-10 family

IFN- β MSYNLIGFLQSSNFQCCOKLMQNLGRLEYCLKDRMNPDIPEETIQLOQFQKEDALTIYENLQNIFAIFRODSSSTGNNETIVENLLANVYHQINHLKTVLEEK

LEKEDPTRGKIMSLHLKRRYGRILHYLKAKESYSHCAWTVIRVEILLRNFFYFINRLTGYLRN

Exemplary protein of the short-chain cytokines family

EPO APPRLICDSRVLEERYLLAKEAENITTTGCAEHCSLNENITVPDTKVNFFAKRMEYGOQAVEWQGLALLSEAVLRGQALLVNSSQPWEPQLQHVDAVSGURSL

TTLLRALGAQKEAISPPDASAAPLRTITADTFPRKLFRRVSNFLRGKLLKYTGACRTGDR

Exemplary protein of the long-chain cytokines family

G-CSF TPLGPASSLPQSFLKLCLEQVRKIQGDGALQEKLVSECATYKLCHEPELVLLGHSIGIPWAPLSSCPSQALQLAGCLSQLHSGLPFLYQGLLQALEGISPEIGPTLDTLQI

DVADFATTIWOQMEELGNAPALQPTQGANPAPASAFQRRAGGVLVASHLQSFLEVSRYVLRHLAQP

FIG. 9